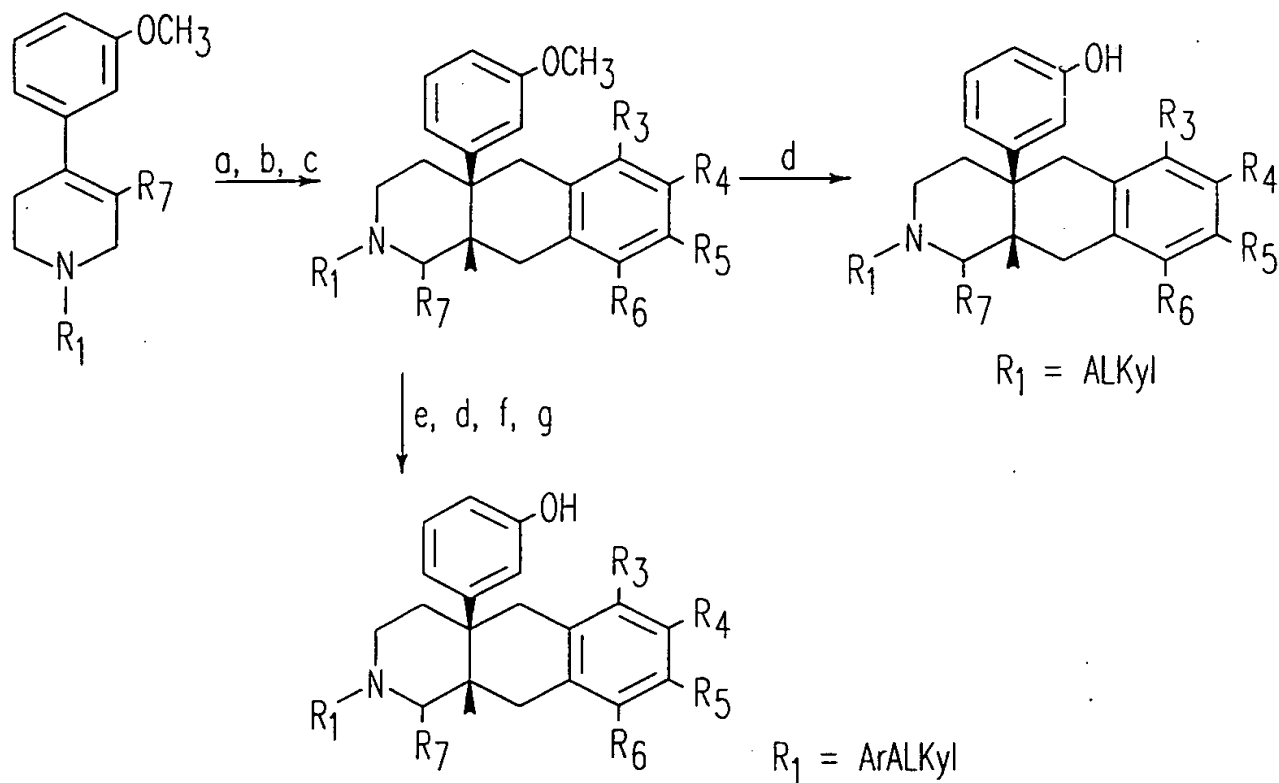
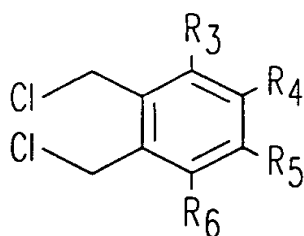


**FIG. 1**



Reagents: (a)  $s\text{-BuLi}$ , THF; AND



(b)  $\text{NaI}$ ,  $\text{CH}_3\text{CN}$ ;

(c)  $\text{NaBH}_4$ ,  $\text{EtOH}$ ;

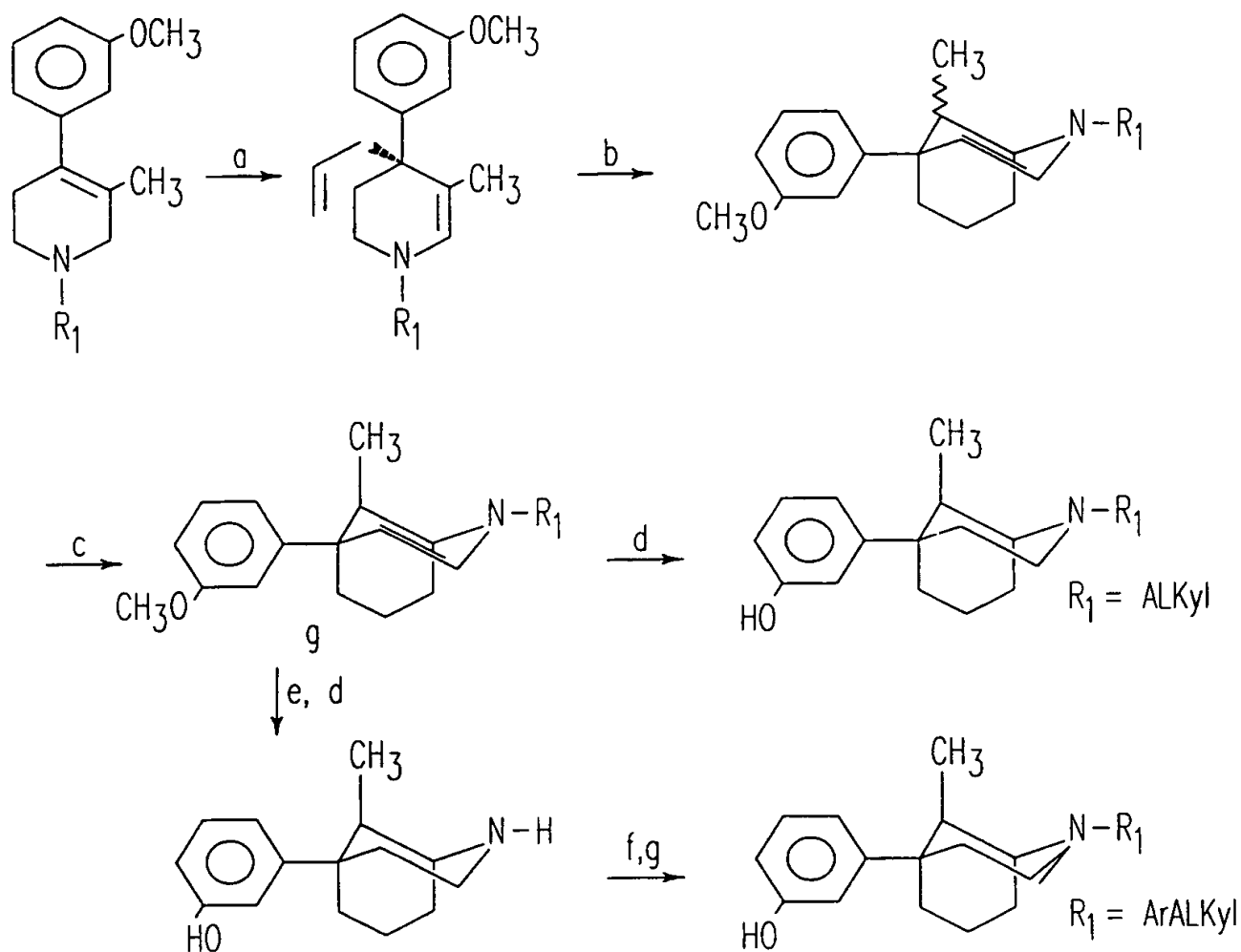
(d)  $\text{HBr}$ ,  $\text{HOAc}$ ;

(e)  $\text{PhOCOC}$ , toluene;

(f) aryl-alkyl- $\text{COOH}$ , BOP, triethylamine, THF,

(g) borane/THF

FIG. 2A



Reagents: (a) s-BuLi, allyl-Br;

(b) H<sub>3</sub>PO<sub>4</sub>, HCO<sub>2</sub>H;

(c) NaHB(OAc)<sub>3</sub>;

(d) HOAc, HBr;

(e) PhOCOCl, then KOH, H<sub>2</sub>O;

(f) BOP, aryl-alkyl-COOH;

(g) borane/THF

FIG. 2B

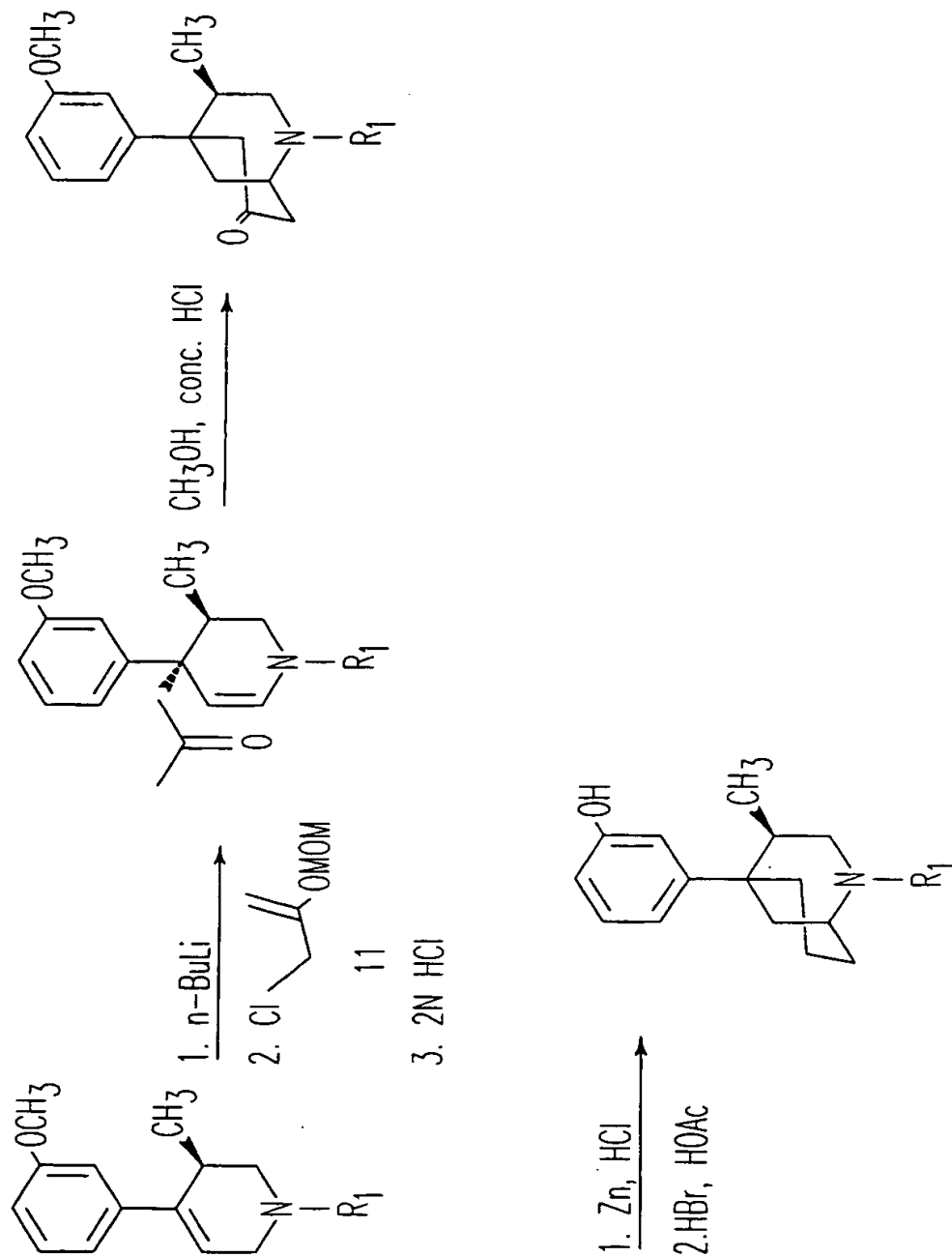
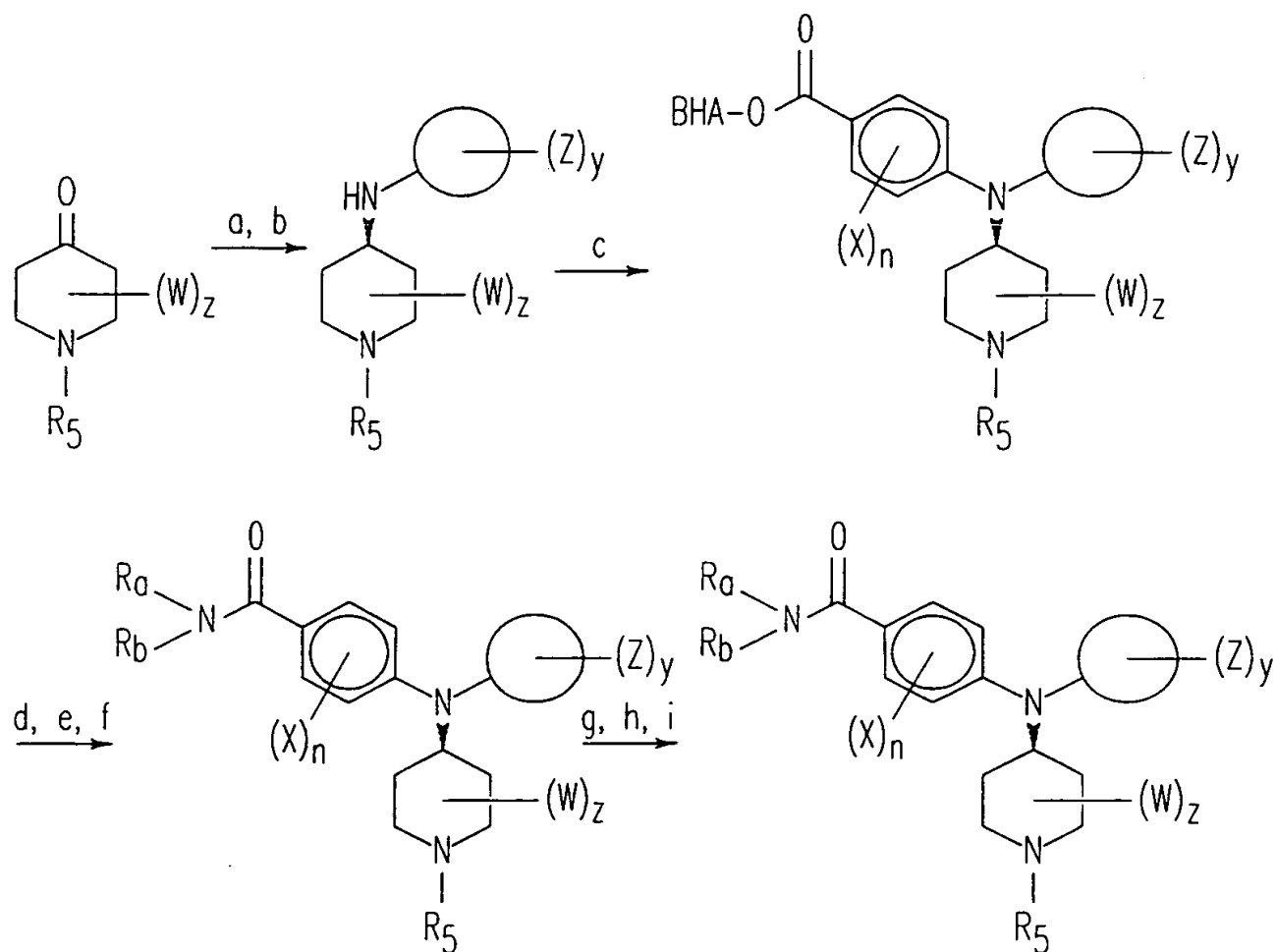
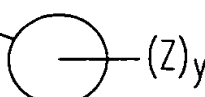




FIG. 4



Reagents: (A)  $Ti(O-i-Pr)_4$ ,  $:NH$    $(Z)_y$

(b)  $NaBH_4$ , EtOH;

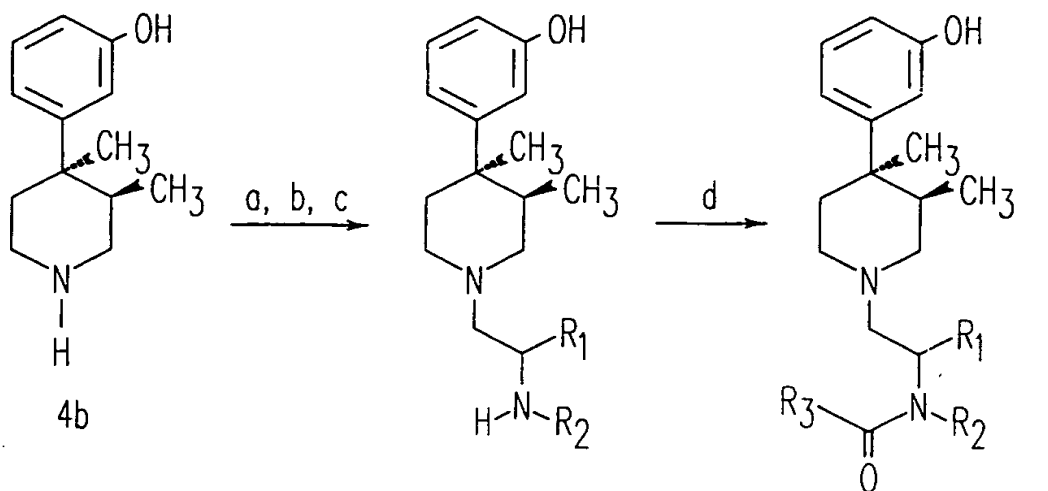
(c)  $n-BuLi$ , THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate;

(d) N-methylpyrrolidinone,  $NaOCH_3$ , toluene; (e) EtOH,  $H_2O$ ;

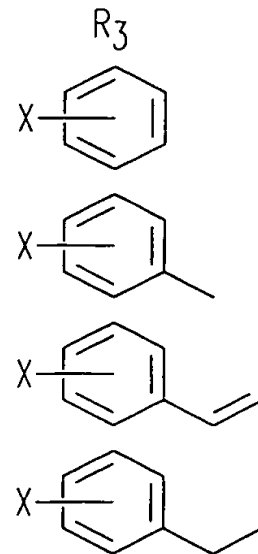
(f)  $R_aR_bNH$ , BOP,  $Et_3N$ ; (g)  $PhOCOCl$ ;

(h)  $KOH$ ,  $i-PrOH$ ,  $H_2O$ ; (i)  $R_5-Br$ , EtOH,  $K_2CO_3$

FIG. 5



	R <sub>1</sub>	R <sub>2</sub>
6a,	H	H
b,	H	CH <sub>3</sub>
c,	CH <sub>3</sub>	H
d,	CH <sub>3</sub>	CH <sub>3</sub>
e,	i-Pr	H
f,	i-Pr	H
g,	i-Bu	H
h,	s-Bu	H
i,	tc-Hex	H
j,	Ph	CH <sub>3</sub>
k,	Bn	H

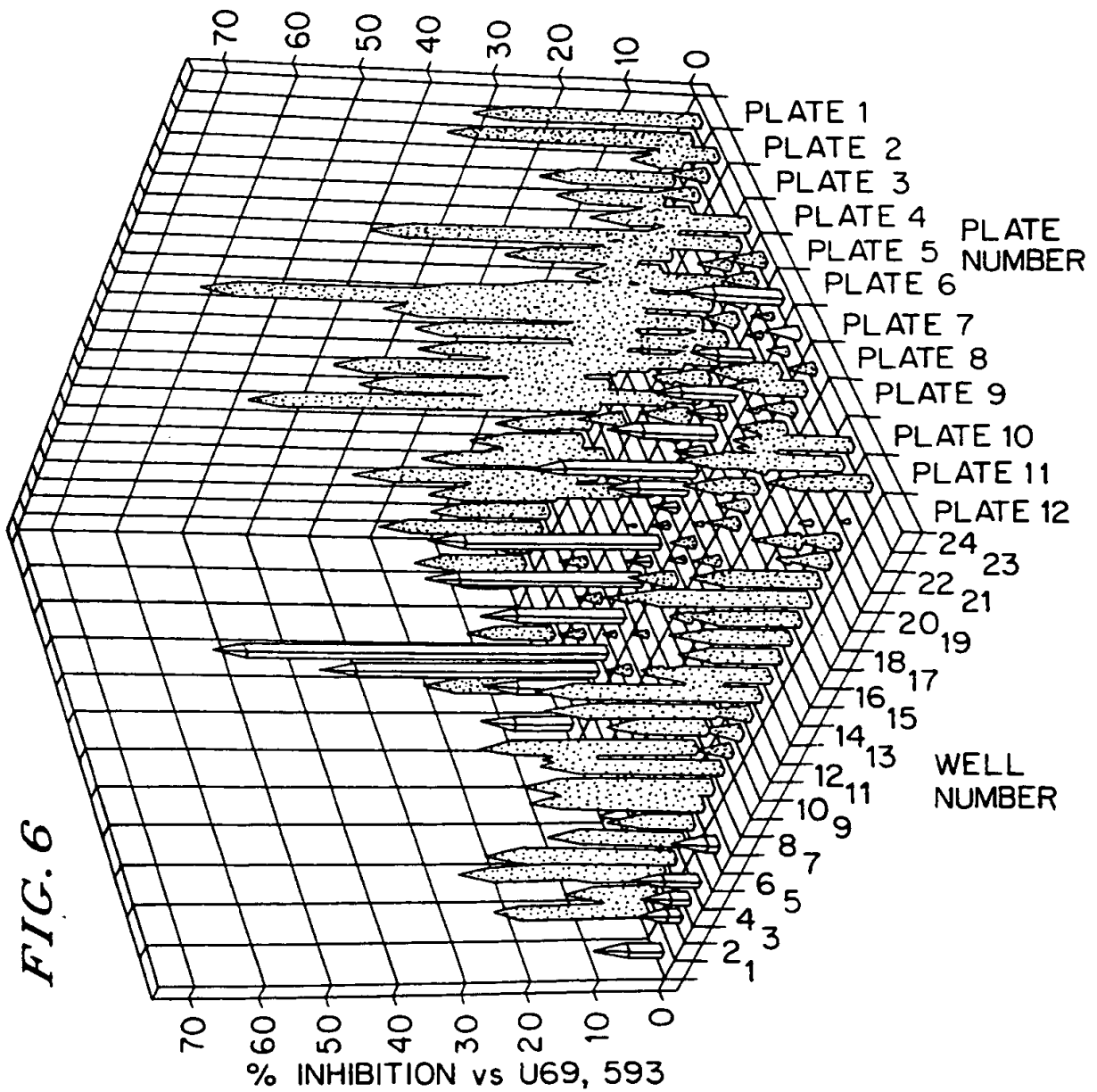


<sup>a</sup> Reagents: (a) Boc-amino acid, BOP, TEA, THF;

(b) TFA, CH<sub>2</sub>Cl<sub>2</sub>;

(c) borane/dimethyl sulfide;

(d) R<sub>3</sub>CO<sub>2</sub>H, BOP, TEA, THF.



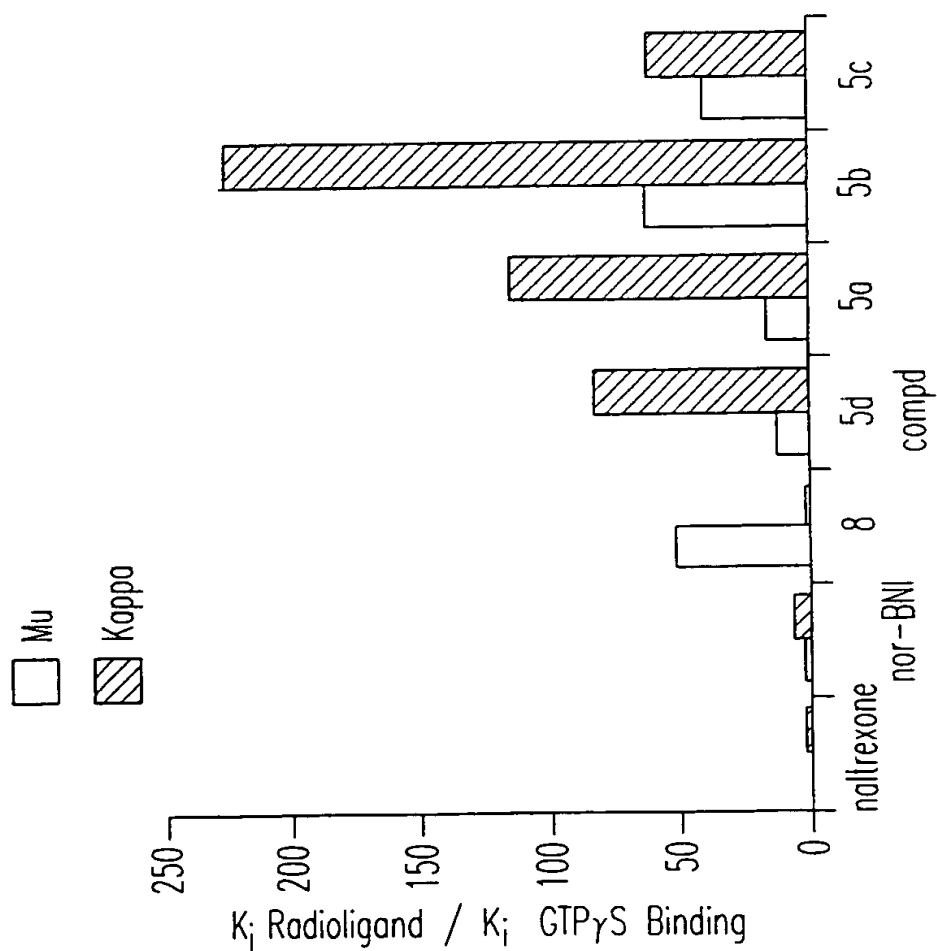
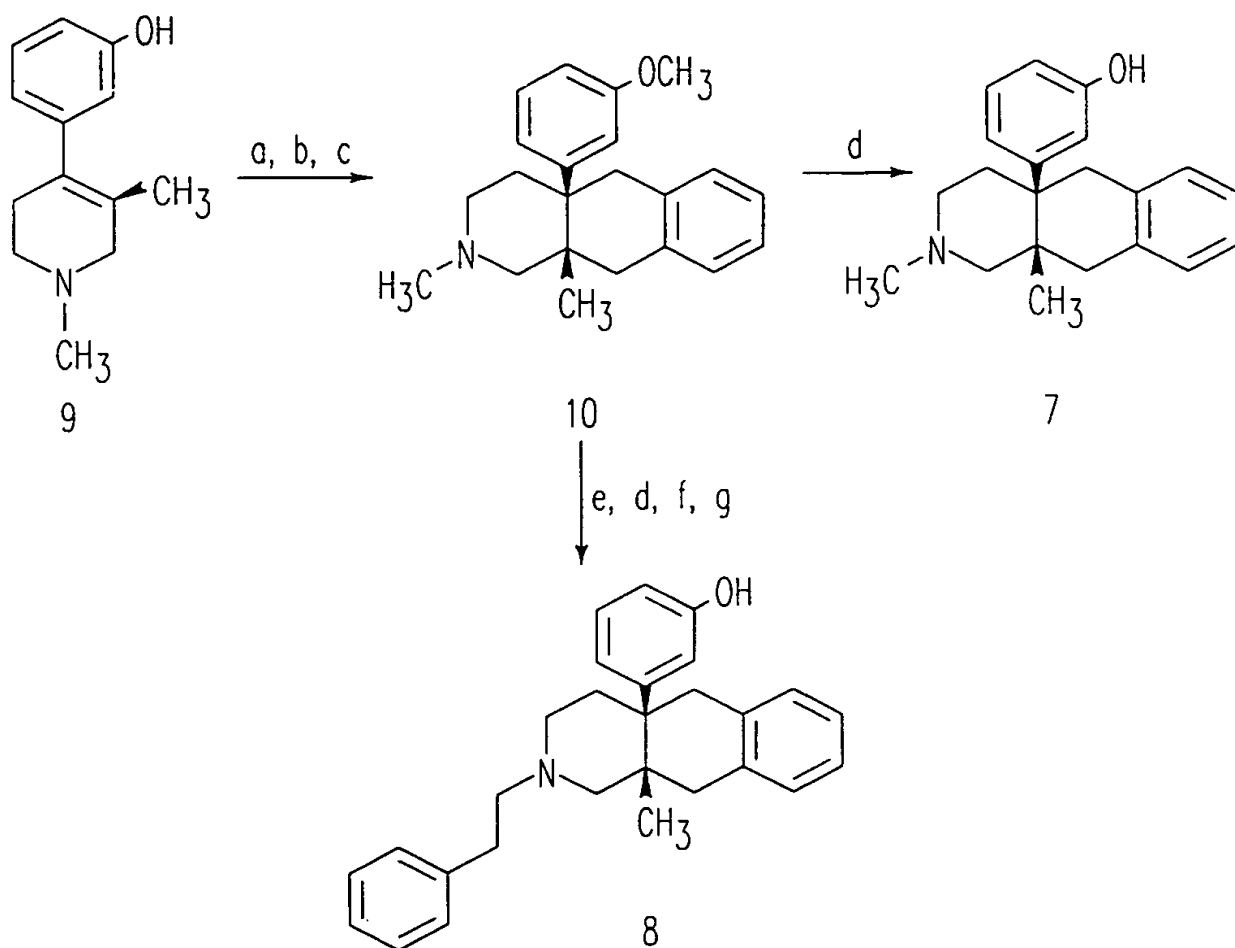


FIG. 7



**FIG. 8**



(a)  $s\text{-BuLi}$ , THF;  $\alpha,\alpha'$ -dichloroxylylene;

(e)  $\text{PhOCOCl}$ , toluene;

(b)  $\text{NaI}$ ,  $\text{CH}_3\text{CN}$ ;

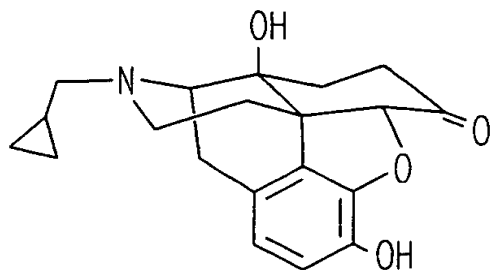
(f) Phenyl Acetic Acid, BOP, TEA, THF;

(c)  $\text{NaBH}_4$ , EtOH;

(g) Borane/THF;

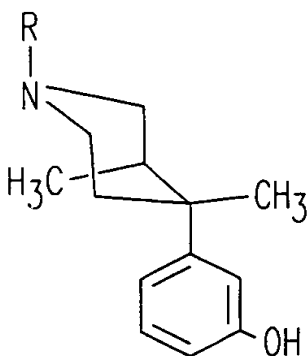
(d)  $\text{HBr}$ ,  $\text{HOAc}$ ;

**FIG. 9A**



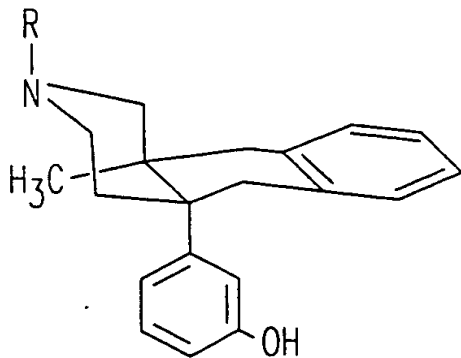
Naltrexone  
(phenylaxial/piperidine chair)

**FIG. 9B**



3,4-Dimethyl-4-(3-hydroxyphenyl)piperidine  
(phenylequatorial/piperidine chair)

**FIG. 9C**



8a-Methyl-4a-(3-hydroxyphenyl)octahydrobenzo[e]isoquinoline  
(phenylequatorial/piperidine chair)

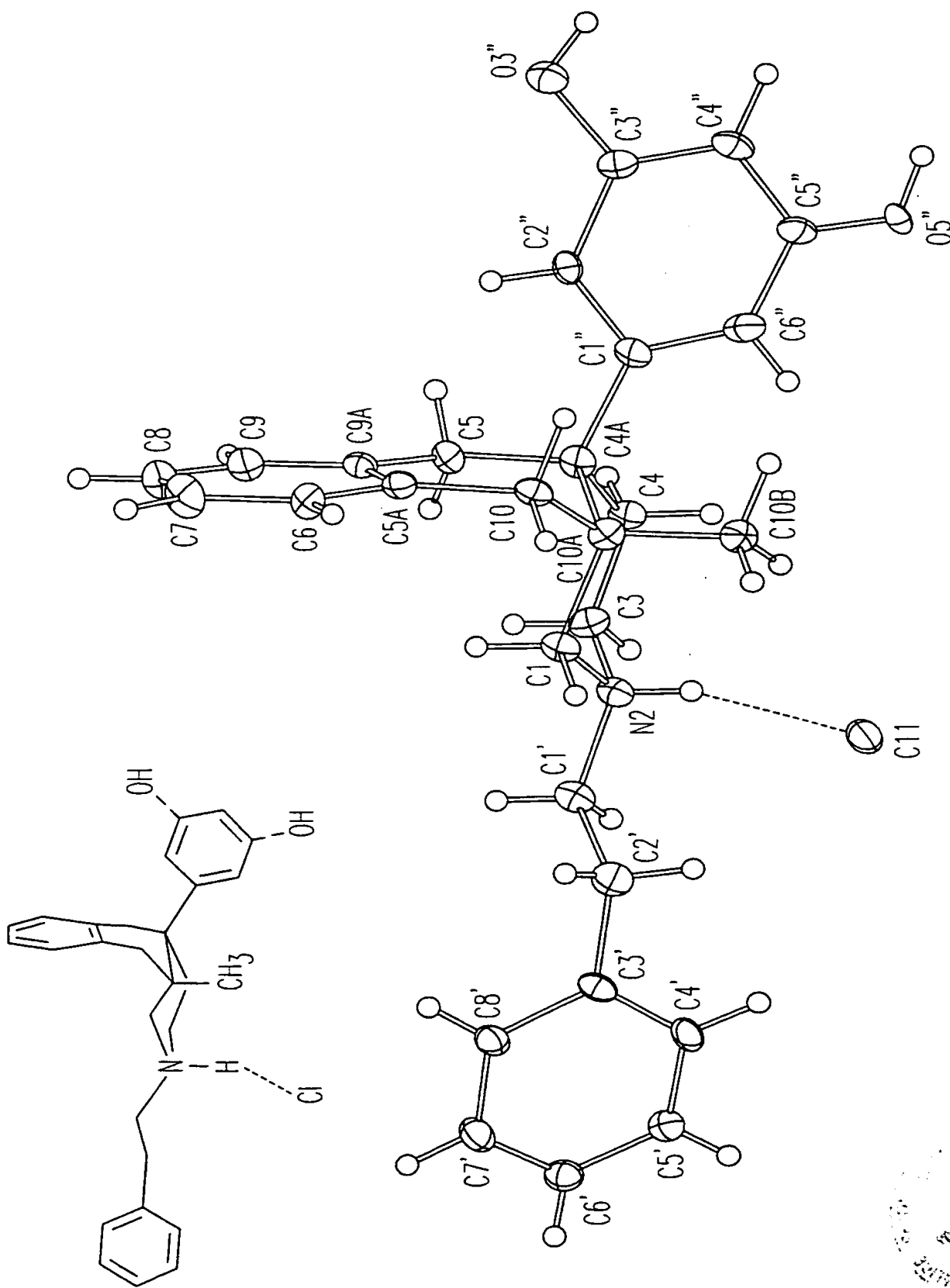


FIG. 11

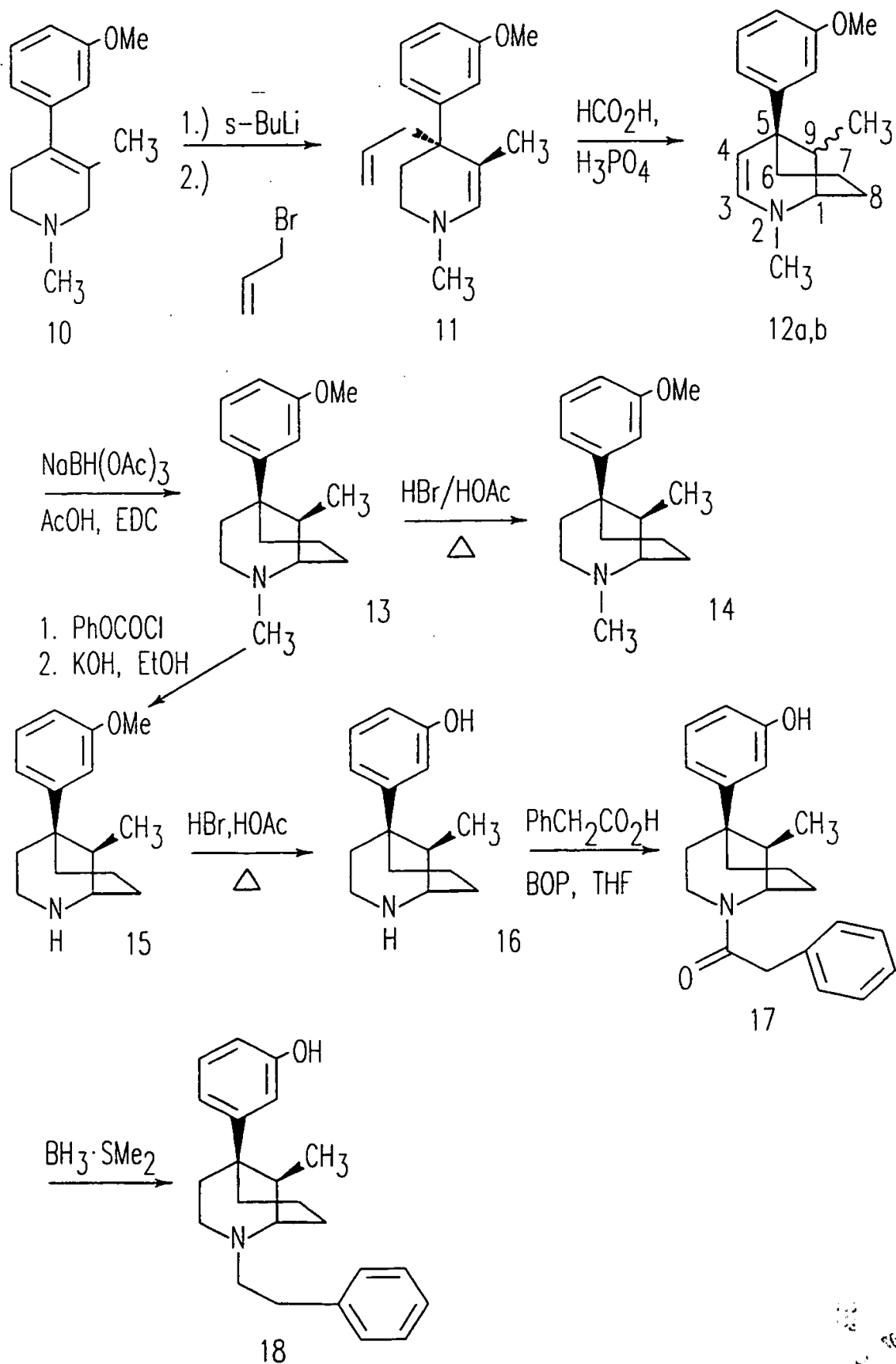


FIG. 12

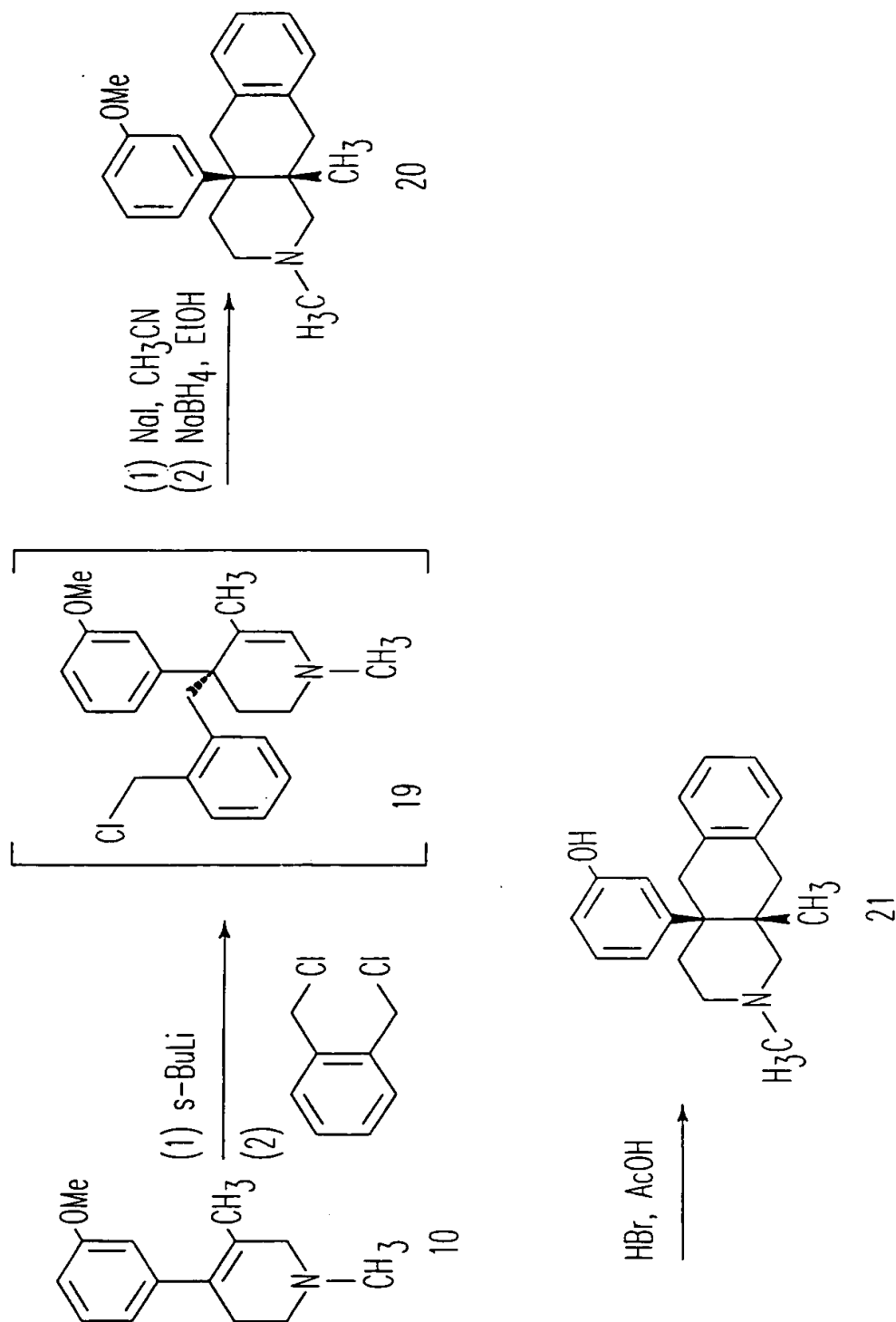
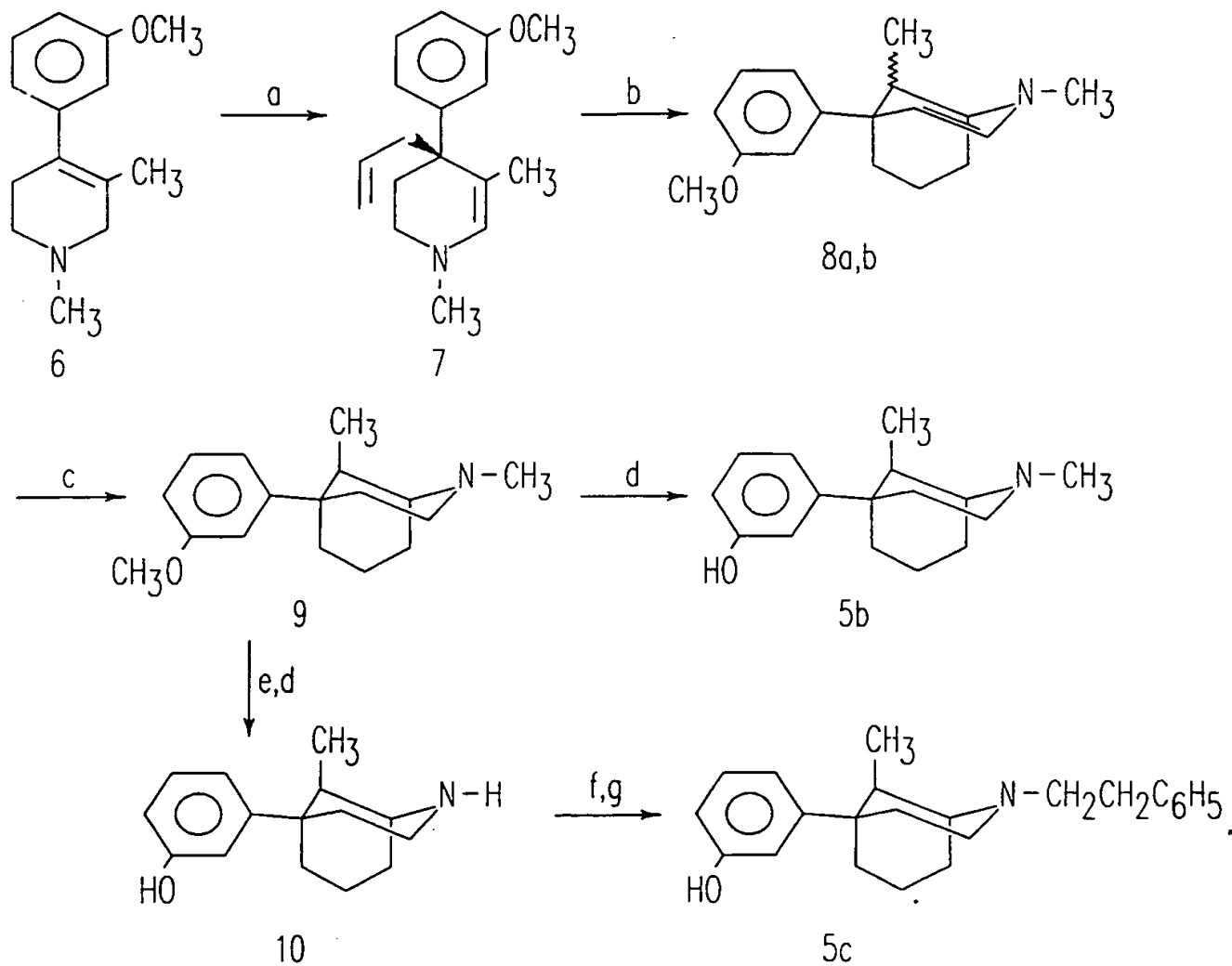


FIG. 13



<sup>a</sup> (a) *s*-BuLi, allyl-Br;

(b) H<sub>3</sub>PO<sub>4</sub>, HCO<sub>2</sub>H;

(c) NaHB(OAc)<sub>3</sub>;

(d) HOAc, HBr;

(e) PhOCOCl, then KOH, H<sub>2</sub>O;

(f) (benzotriazol-1-yloxy)tris(dimethylamino) phosphonium hexafluorophosphate, PhCH<sub>2</sub>CO<sub>2</sub>H;

(g) borane-dimethyl sulfide, THF.

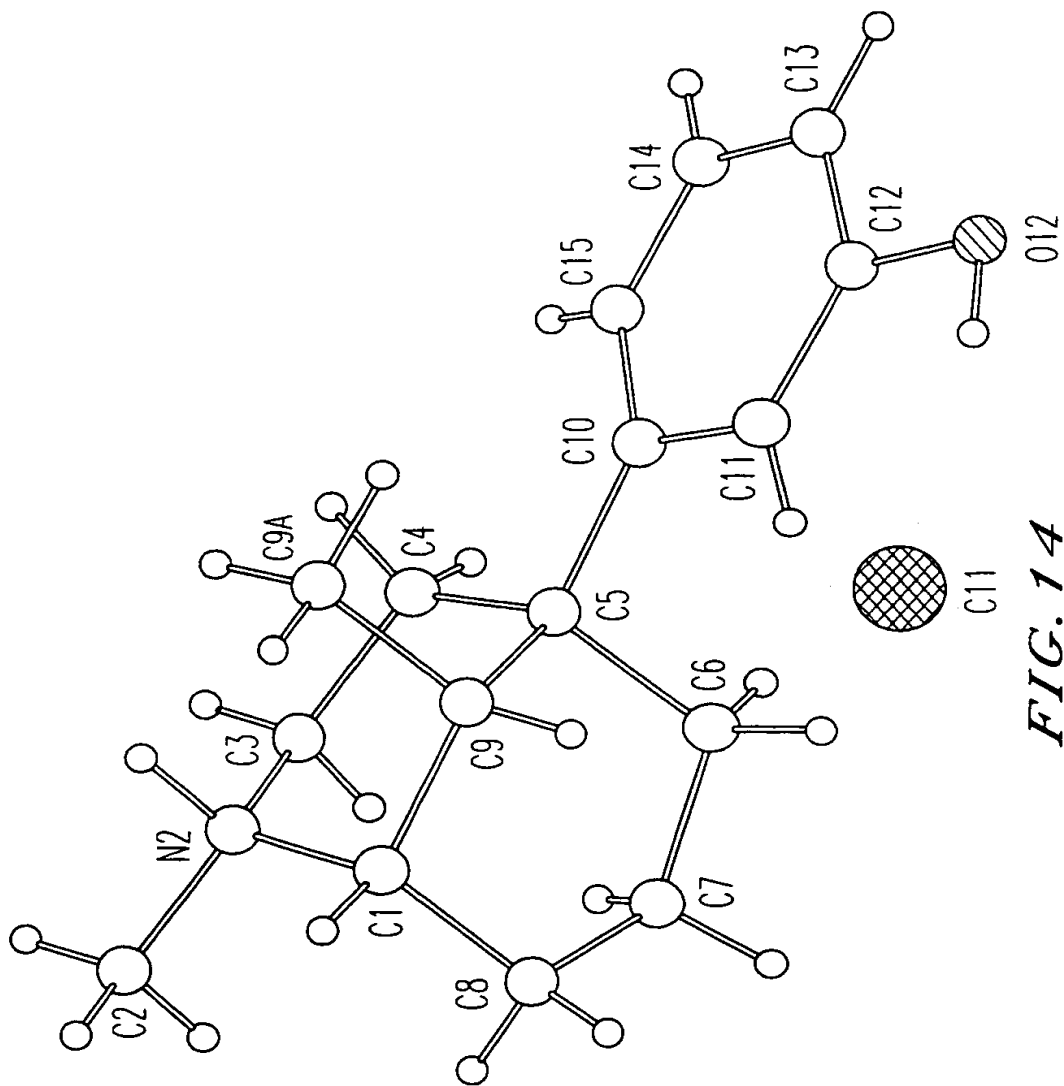
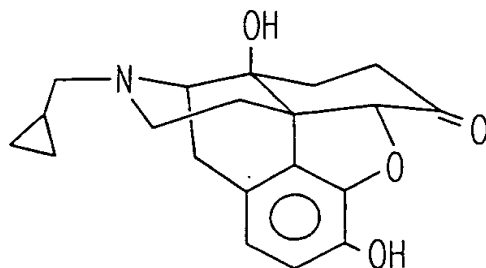


FIG. 14

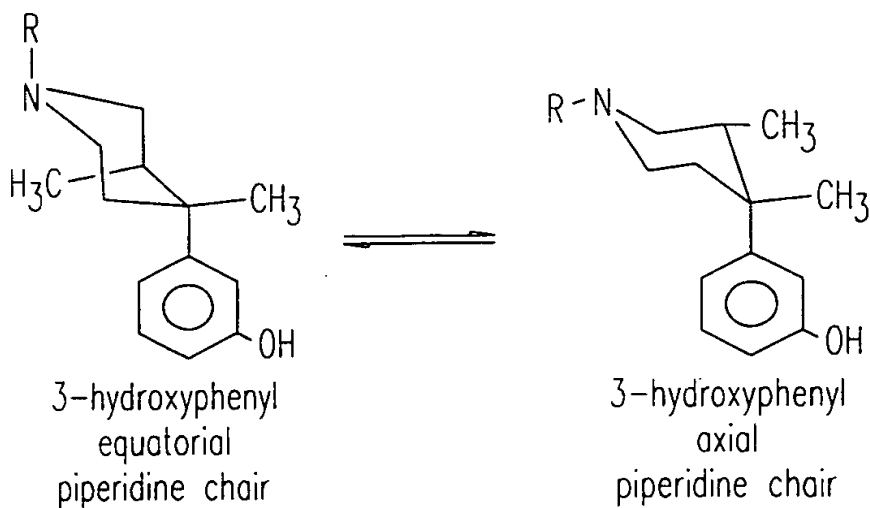
# FIG. 15

Naltrexone (1b)

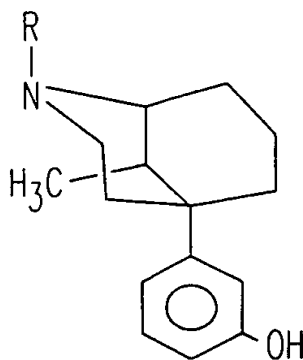


3-hydroxyphenyl axial piperidine chair

3,4-Dimethyl-4-(3-hydroxyphenyl)-piperidine (4)



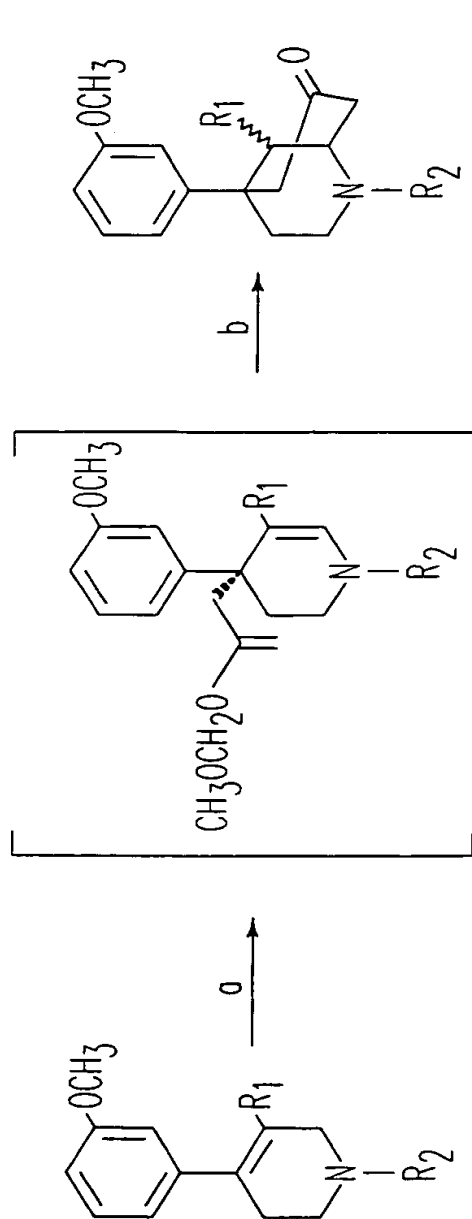
2-Alkyl-9 $\beta$ -methyl-5-(3-hydroxyphenyl)-  
morphan (5)



3-hydroxyphenyl equatorial piperidine chair



FIG. 16



15a, R<sub>1</sub> = CH<sub>3</sub>, R<sub>2</sub> = CH<sub>3</sub>  
15b, R<sub>1</sub> = H, R<sub>2</sub> = Et  
15c, R<sub>1</sub> = H, R<sub>2</sub> = Bn

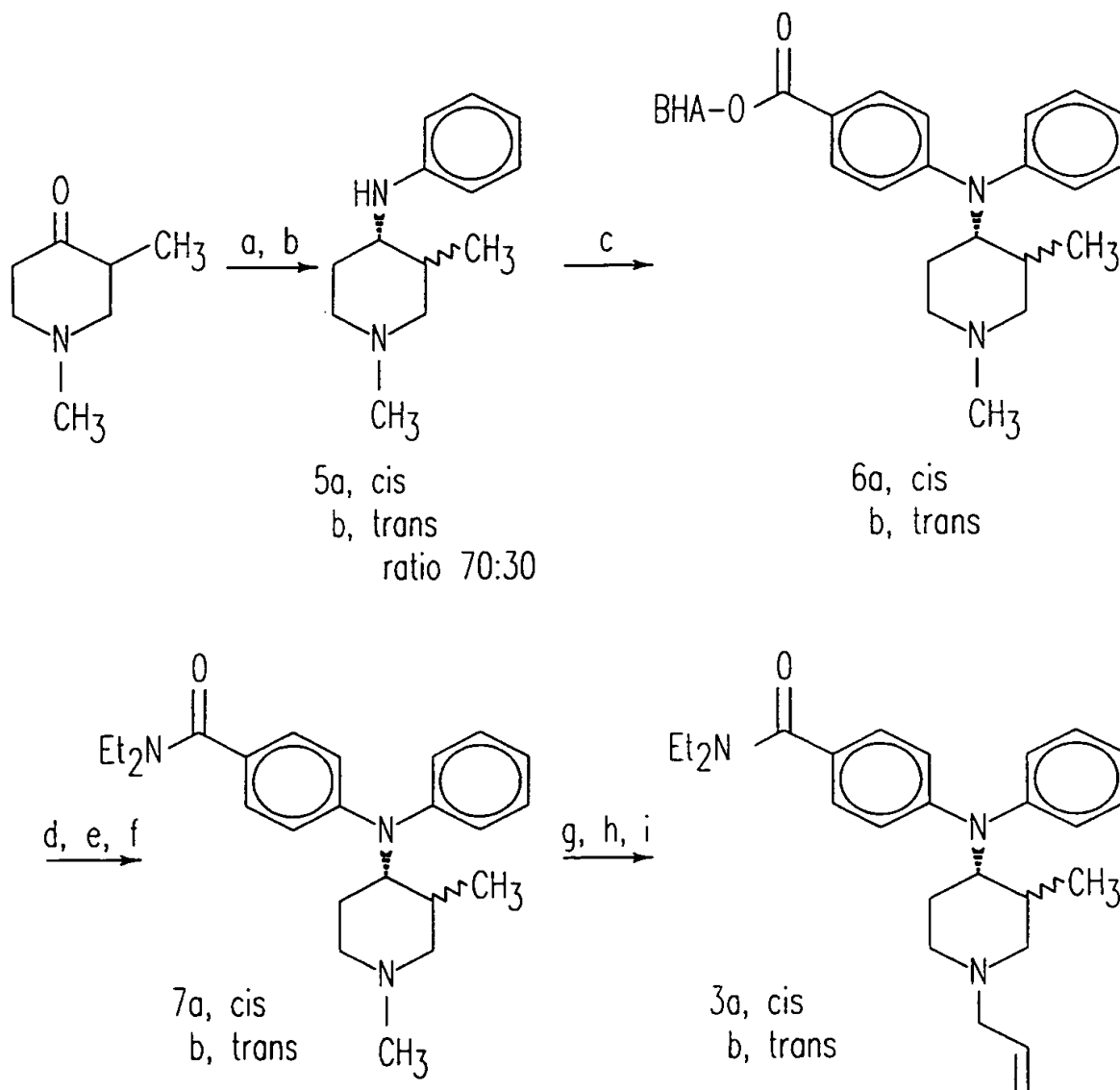
16a, R<sub>1</sub> = CH<sub>3</sub>, R<sub>2</sub> = CH<sub>3</sub>  
16b, R<sub>1</sub> = H, R<sub>2</sub> = Et  
16c, R<sub>1</sub> = H, R<sub>2</sub> = Bn

17a, R<sub>1</sub> = BCH<sub>3</sub>, R<sub>2</sub> = CH<sub>3</sub>  
17b, R<sub>1</sub> = H, R<sub>2</sub> = Et  
17c, R<sub>1</sub> = H, R<sub>2</sub> = Bn  
17d, R<sub>1</sub> = αCH<sub>3</sub>, R<sub>2</sub> = CH<sub>3</sub>

(a) R<sub>1</sub> = H, n-BuLi ; CH<sub>3</sub>OCH<sub>2</sub>O — (b) 6N HCl, THF  
R<sub>1</sub> = CH<sub>3</sub>, s-BuLi  
TMEDA

18

FIG. 17



Reagents: (a) Ti(O-i-Pr)<sub>4</sub>, aniline; (b) NaBH<sub>4</sub>, EtOH; (c) n-BuLi, THF, HMPA then 1-(2,6-di-tert-butyl-4-methoxy)-4-fluorobenzoate; (d) N-methylpyrrolidinone, NaOCH<sub>3</sub>, toluene; (e) EtOH, H<sub>2</sub>O; (f) Et<sub>2</sub>NH, BOP, Et<sub>3</sub>N; (g) PhOCOCl; (h) KOH, i-PrOH, H<sub>2</sub>O; (i) allyl-Br, EtOH, K<sub>2</sub>CO<sub>3</sub>

FIG. 18

